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Combination pharmacotherapy for the management of pain (2008)

Submission date
29/07/2009

Registration date
03/08/2009

Last Edited
05/05/2016

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
MCT-94187; ANAE-151-09

Study information

Scientific Title

A double-blind, randomised controlled trial of nortriptyline, morphine, and their combination for neuropathic pain

Study objectives
A combination of morphine and nortriptyline has superior analgesic efficacy versus either drug alone for reducing neuropathic pain.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Queen's University Research Ethics Board, 23/03/2009

Study design
Double-blind randomised three-period crossover trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neuropathic pain

Interventions
1. Morphine-nortryptyline combination
2. Morphine
3. Nortriptyline

As per a double-dummy, balanced Latin Square design, trial medications are administered orally in three different treatment periods. In each of the three periods, doses of nortriptyline, morphine and the two in combination are gradually titrated - over 24 days - towards each individual maximal tolerated dose and continued at that dose for seven days followed by an 11 day taper-washout period. Ceiling doses are 100 mg daily for both nortriptyline and morphine. Total duration of follow-up is 8 months.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Morphine, nortriptyline

Primary outcome(s)
Daily pain intensity. Patient follow-up for primary and secondary outcomes were recorded during treatment at maximal tolerated dose (i.e. day 25 - 31) for each treatment period.

Key secondary outcome(s))
1. Global pain relief, measures of sedation, constipation, other side effects and maximal tolerated drug doses
2. Short form McGill Pain Questionnaire-2
3. Brief Pain Inventory
4. Beck Depression Inventory
5. 36-item short form health survey (SF-36)
6. Blinding questionnaires
7. Acetaminophen consumption
8. Serum drug levels

Daily pain intensity. Patient follow-up for primary and secondary outcomes were recorded during treatment at maximal tolerated dose (i.e. day 25 - 31) for each treatment period.

Completion date
30/10/2012

Eligibility

Key inclusion criteria
1. Neuropathic pain
2. Daily moderate (greater than or equal to 4/10) pain for at least 3 months
3. Adults aged 18 to 89 years, either sex
4. Liver function tests: alanine aminotransferase (ALT), aspartate aminotransferase (AST) less than 1.2 times upper limit of normal
5. Creatinine less than 1.5 times upper limit of normal
6. Negative serum beta-human chorionic gonadotrophin (B-HCG) for women of childbearing potential
7. Adequate birth control for all women of child-bearing potential
8. Sufficient cognitive function, visual acuity and English language skills to complete questionnaires and communicate verbally with the nursing staff to permit titration of the study drugs

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. Painful condition as severe as, but distinct from presenting neuropathic pain
2. Pregnancy or lactation
3. End-stage kidney or liver disease
4. Moderate to severe heart disease (myocardial infarction [MI] within preceding year, unstable angina, cardiac conduction defect or congestive heart failure)
5. Cardiovascular autonomic neuropathy
6. Postural hypotension greater than 20 mmHg on initial assessment
7. Males with urinary symptoms attributable to benign prostatic hypertrophy
8. Patients who live alone and cannot assure daily contact with a friend, family member or caregiver
9. Angle-closure glaucoma
10. Ongoing administration of monoamine oxidase inhibitors, serotonin-specific reuptake inhibitors, serotonin-norepinephrine inhibitors
11. Any serious psychiatric disorder as diagnosed by a psychiatrist (including bipolar disorder)
12. Seizure disorder
13. Ongoing administration of anticonvulsants which induce cytochrome P450 enzymes (e.g. carbamazepine, oxcarbazepine, barbiturates and phenytoin) as well as rifampin
14. Hypersensitivity to, or previous intolerability of, any of the study medications
15. History of significant abuse of illicit drugs, prescription drugs or alcohol

Date of first enrolment
01/11/2009

Date of final enrolment
30/10/2012

Locations

Countries of recruitment
Canada

Study participating centre
Kingston General Hospital
Kingston
Canada
K7L 2V7

Sponsor information

Organisation
Queen's University (Canada)

ROR
https://ror.org/02y72wh86

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: MCT-94187)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes